the second component is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof.

42. (Amended) The method of Claim 39, wherein the first component comprises parthenolide; and

the second component is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof.

REMARKS

In the communication referred above, the Examiner has required restriction to one of 20 inventions:

Group I (Claims 1-5), drawn to a composition for inhibition of COX-2 activity comprising a sesquiterpene lactone and diterpene lactone or triterpene, classified in Class 424, subclass 725, for example;

Group II (Claims 6-9), drawn to a composition for inhibition of COX-2 activity comprising a first compound, such as encelin, and a second component, such as betulin, classified in Class 424, subclass 775, for example.

Group III (Claims 11-15), drawn to a composition for inhibition of COX-2 activity comprising a first compound, such as melapodin A, and a second compound, such as glycyrrhizic acid, classified in Class 424, subclass 725, for example.

Group IV (Claims 16-20), drawn to a composition for inhibition of COX-2 comprising parthenolide and a compound, such as ursolic acid, classified in Class 424, subclass 732, for example.

Group V (Claims 21-25), drawn to a method of dietary supplementation comprising administration of a sesquiterpene lactone and diterpene lactone or triterpene, classified in Class 558, subclass 12, for example.

Group VI (Claims 26-28), drawn to a method of dietary supplementation comprising administration of a composition comprising constituents, such as tenulin and betulin, classified in Class 558, subclass 310, for example.

Group VII (Claim 29), drawn to a method of dietary supplementation comprising administration of a composition comprising constituents, such as melapodin A and dehydroandrographolide, classified in Class 560, subclass 249, for example.

Group VIII (Claim 30), drawn to a method of dietary supplementation comprising administration of a composition comprising constituents, such as parthenolide and oleanolic acid, classified in Class 424, subclass 728, for example.

Group IX (Claim 31), drawn to a method for therapeutic treatment comprising administration of a sesquiterpene lactone and diterpene lactone or triterpene, classified in Class 540, subclass 41, for example.

Group X (Claim 32), drawn to a method for therapeutic treatment comprising administration of a composition comprising constituents, such as leucanthin B and triperin, classified in Class 514, subclass 783, for example.

Group XI (Claim 33), drawn to a method for therapeutic treatment comprising administration of a composition comprising constituents, such as encelin and oleanolic acid, classified in Class 552, subclass 293, for example.

Group XII (Claim 34), drawn to a method for therapeutic treatment comprising administration of a composition comprising parthenolide and andrographolide, classified in Class 424, subclass 774, for example.

Group XIII (Claim 35), drawn to a method for therapeutic treatment comprising administration of a sesquiterpene lactone and diterpene lactone or triterpene, classified in Class 540, subclass 115, for example.

Group XIV (Claim 36), drawn to a method for therapeutic treatment comprising administration of a composition comprising constituents, such as psilostachyin A and deoxyandrographolide, classified in Class 424, subclass 764, for example.

Group XV (Claim 37), drawn to a method for therapeutic treatment comprising administration of a composition comprising parthenolide and glycyrrhetinic acid, classified in Class 424, subclass 773, for example.

Group XVI (Claim 38), drawn to a method for therapeutic treatment comprising administration of parthenolide and ursolic acid, classified in Class 424, subclass 732, for example.

Group XVII (Claim 39), drawn to a method for therapeutic treatment comprising administration of a sesquiterpene lactone and diterpene lactone or triterpene, classified in Class 549, subclass 263, for example.

Group XVIII (Claim 40), drawn to a method for therapeutic treatment comprising administration of a composition comprising constituents, such as confertiflorin and betulinic acid, classified in Class 514, subclass 175, for example.

Group XIX (Claim 41), drawn to a method for therapeutic treatment comprising administration of a composition comprising constituents, such as melapodin A and glycyrrhizic acid, classified in Class 424, subclass 769, for example.

Group XX (Claim 42), drawn to a method for therapeutic treatment comprising administration of parthenolide and andrographolide, classified in Class 514, subclass 783, for example.

Applicants hereby elect, without traverse, to prosecute the claims directed to Group 1, classified in Class 424, Subclass 725, in the present application. Applicants reserve the right to pursue the remaining claims in a divisional application. Accordingly, prompt examination on the merits of Claims 1-5 is respectfully requested.

Upon allowance of the elected claims drawn to the product, Applicants respectfully request rejoinder of Claims 21-25, in accordance with M.P.E.P. 821.04. That section of the M.P.E.P. states that if

Applicants elect claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. Amended Claims 21-25 are drawn to a method of dietary supplementation comprising administration of the composition of Claim 1. Accordingly, rejoinder of these claims will be appropriate in accordance with M.P.E.P. 821.04.

Additionally, Claims 6, 11, 16, 26, and 29-40 have been amended such that Claims 6-20 and 26-42 are ultimately dependent on Claim 1. According to M.P.E.P. 809.03, there are a number of situations which arise in which an application has claims to two or more properly divisible inventions, so that a requirement to restrict the application to one would be proper, but presented in the same case are one or more claims (generally called "linking" claims) inseparable therefrom and thus linking together the inventions otherwise divisible. As amended, Claims 6, 11, 16, 26, and 29-40 are linking claims and are generic to and link their corresponding groups to Group I. Accordingly, upon allowance of Claim 1, Applicants respectfully request that the restriction requirement be withdrawn as to the linked inventions and any claims containing all of the limitations of Claim 1, i.e. all of the pending claims.

The title has been amended to correct a typographical error. Accordingly, no new matter has been added.

The specific changes to the specification and amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment and Response to Restriction Requirement. On this page, the insertions are underlined while **[the deletions are bolded and bracketed]**.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: November 12, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please amend the title as follows:

COMBINATIONS OF SESQUITERPENE LACTONES AND **[DITEPENE]** DITERPENE LACTONES OR TRITERPENES FOR SYNERGISTIC INHIBITION OF CYCLOOXYGENASE-2

IN THE CLAIMS:

Please amend Claims 6, 11, 16, 21, 22, 26, 27, and 29-42 as follows:

6. (Amended) A composition **[for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising, as a]** of Claim 1, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, melapodin A, tenulin, confertiflorin, burrodin, psilostachyin A, costunolide, strigol, and helenalin; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, aneoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof.

11. (Amended) A composition **[for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising, as a]** of Claim 1, wherein, the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, and melapodin A; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof.

16. (Amended) A composition **[for inhibition of inducible COX-2 activity and having minimal effect on COX-1 activity, said composition comprising, as a]** of Claim 1, wherein, the first component **[an effective amount of a pharmaceutical grade]** comprises parthenolide and **[a]** the

second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof.

21. (Amended) A method of dietary supplementation in animals comprising administering to an animal suffering symptoms of inflammation a composition **[comprising, as a first component an effective amount of a sesquiterpene lactone species and an effective amount of a second component selected from the group consisting of a diterpene lactone species and a triterpene species or derivatives thereof,]** of Claim 1 and continuing said administering of the composition until said symptoms are reduced.

22. (Amended) The method of Claim 21 wherein the composition is formulated in a dosage form such that said administration provides from 0.05 to 5.0 mg body weight per day of each **[sequesterpene]** sesquiterpene lactone species, and from 0.5 to 20.0 mg/kg bodyweight per day of each diterpene lactone species or triterpene species.

26. (Amended) **[A]** The method of **[dietary supplementation in animals comprising administering to an animal suffering symptoms of inflammation a composition comprising, as a]** Claim 21, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, melapodin A, tenulin, confertiflorin, burrodin, psilostachyin, A, costunolide, strigol, and helenalin; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, aneoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

27. (Amended) The method of Claim 26 wherein the composition is formulated in a dosage form such that said administration provides from 0.05 to 5.0 mg body weight per day of each **[sequesterpene]** sesquiterpene lactone species, and from 0.5 to 20.0 mg/kg bodyweight per day of each diterpene lactone species or triterpene species.

29. (Amended) **[A]** The method [dietary supplementation in animals comprising administering to an animal suffering symptoms of inflammation a composition comprising, as a] of Claim 21, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, and melapodin

A; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

30. (Amended) **[A]** The method of **[dietary supplementation in animals comprising administering to an animal suffering symptoms of inflammation a composition comprising, as a]** Claim 21, wherein the first component **[an effective amount of a pharmaceutical grade]** comprises parthenolide and; **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

31. (Amended) **[A]** The method therapeutic treatment in animals comprising administering to an animal suffering symptoms of arthritis a composition **[comprising, as a first component an effective amount of sesquiterpene lactone species and an effective amount of a second component selected from the group consisting of a diterpene lactone species and a triterpene species or derivatives thereof,]** of Claim 1 and continuing said administering of the composition until said symptoms are reduced.

32. (Amended) **[A]** The method of **[therapeutic treatment in animals comprising administering to an animal suffering symptoms of arthritis a composition comprising, as a]** of Claim 31, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, melapodin A, tenulin, confertiflorin, burrodin, psilostachyin A, costunolide, strigol, and helenalin; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

33. (Amended) **[A]** The method of **[therapeutic treatment in animals comprising administering to an animal suffering symptoms of arthritis a composition comprising, as a]** of

Claim 31, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, and melapodin A; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

34. (Amended) **[A]** The method of **[therapeutic treatment in animals comprising administering to an animal suffering symptoms of arthritis a composition comprising, as a]** of Claim 31, wherein the first component **[an effective amount of a pharmaceutical grade]** comprises parthenolide and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

35. (Amended) A method of therapeutic treatment comprising applying to the skin of a human suffering symptoms of acne rosacea a lotion comprising a composition **[comprising, as a first component an effective amount of a sesquiterpene lactone species and an effective amount of a second component selected from the group consisting of a diterpene lactone species and a triterpene species or derivatives thereof,]** of Claim 1 and continuing said administering of the composition until said symptoms are reduced.

36. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms of acne rosacea a lotion comprising a composition comprising, as a]** Claim 35, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, melapodin A, tenulin, confertiflorin, burrodin, psilostachyin A, costunolide, strigol, and helenalin; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

37. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms of acne rosacea a lotion comprising a composition comprising, as a]** Claim 35, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, and melapodin A; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

38. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms of acne rosacea a lotion comprising a composition comprising, as a]** Claim 35, wherein the first component **[an effective amount of a pharmaceutical grade]** comprises parthenolide and **[a]** second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

39. (Amended) A method of therapeutic treatment comprising applying to the skin of a human suffering symptoms of psoriasis a lotion comprising a composition **[comprising, as a first component an effective amount of sesquiterpene lactone species and an effective amount of a second component selected from the group consisting of a diterpene lactone species and a triterpene species or derivatives thereof,]** of Claim 1 and continuing said administering of the composition until said symptoms are reduced.

40. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms of psoriasis a lotion comprising a composition comprising, as a]** of Claim 39, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, melapodin A, tenulin, confertiflorin, burrodin, psilostachyin A, costunolide, strigol, and helenalin; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid,

glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

41. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms of psoriasis a lotion comprising a composition comprising, as a]** Claim 39, wherein the first component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of parthenolide, encelin, leucanthin B, enhydrin, and melapodin A; and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, dehydroandrographolide, deoxyandrographolide, neoandrographolide, ursolic acid, oleanolic acid, betulin, betulinic acid, glycyrrhetinic acid, glycyrrhizic acid, triperin, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.

42. (Amended) **[A]** The method of **[therapeutic treatment comprising applying to the skin of a human suffering symptoms psoriasis a lotion comprising a composition comprising, as a]** of Claim 39, wherein the first component **[an effective amount of a pharmaceutical grade]** comprises parthenolide and **[a]** the second component **[an effective amount of a pharmaceutical grade compound]** is selected from the group consisting of andrographolide, ursolic acid, oleanolic acid, and derivatives thereof **[, and continuing said administering of the composition until said symptoms are reduced]**.